IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit	: 1645	**Customer No.: 035811**
Examiner	: Jana A. Hines	
Serial No.	: 10/795,873	
Filed	: March 8, 2004	
Inventors	: Jean-Pierre Hermet	Docket No.: 1049-04
	: Isabelle Besson-Faure	
	: Sébastien Ribault	Confirmation No.: 3189
	: Yann Godfrin	
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Title	: DEVICE AND METHOD FOR	
	: CONCENTRATING AND DETECTING	
	: PATHOGENIC MICROBES FROM BLOOD	
	: PRODUCTS AND/OR THEIR DERIVATIVES	
		Dated: December 1, 2009

RESPONSE

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
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Sir:

This is submitted in response to the Official Action dated August 6, 2009.

Claims 1- 5, 8, 10, 14 – 17, 23 – 27 and 37 – 38 stand rejected under 35 USC §103 over the hypothetical combination of Zierdt and Aunet and Doshi. The Applicants respectfully submit that one skilled in the art would not make this hypothetical combination, but in any event, the methodology resulting from that combination would still be quite different from the subject matter of the above-mentioned claims. Reasons are set forth below.

The rejection frankly acknowledges that Doshi does not disclose performing the method in an enclosed and sterile device and comprising selectively lysing the cells and recovering microbes with a second filter having a pore size of about 0.3 µm to less than 1 µm which retains contaminating microbes and allows passage of cellular debris. The Applicants agree. Instead, Doshi, for example, does not disclose, teach or suggest that a lysis step is applied to the blood

sample. At most, Doshi refers to the measurement of various variables in the Doshi process such as the amount of plasma, efficiency of filtration and any blood cells that have expired during the process. However, there is no step of conducting lysis. In fact, Doshi leads away from such a step.

In Doshi, the purpose of the agglutination step is to rid the resulting sample of red blood cells (or parts thereof). Doshi clearly speaks to this aspect when it discusses the second filter (col. 12, line 1). If extra red blood cells escape the first step, a second filter can be added to trap the red blood cells remaining while allowing the plasma to pass through. Adding a lysis step at this point would frustrate that purpose as flowing through the filter would be the red blood cell components as well. Hence, one skilled in the art would not want to add a lysis step in Doshi.

The rejection therefore turns to Zierdt to cure this deficiency and refers to page 74, col. 2 and page 75, col. 1 for the proposition that Zierdt teaches selectively lysing the cells and recovering microbes with a second filter having a pore size of about 0.3 μm to less than 1 μm which retains contaminating microbes and allows passage of cellular debris.

On the one hand, Zierdt discloses a lysis-filtration culture technique. Lysis is disclosed as allowing for the separation of bacterial pathogens from antibacterial properties of the blood on page 74 in the first paragraph. On the other hand, page 75, col. 1 refers to lysis of blood samples with a blood lysing solution. However, that lysis refers to the entire blood sample.

This is sharply contrasted to the Applicants' claimed method which selectively lyses residual cells of the filtrate. In other words, there is a first filter step and then only residual cells of the filtrate are lysed and then subjected to a second filtration step. The Applicants respectfully submit that Zierdt fails to disclose, teach or suggest filtration of residual cells. Instead, the entire sample is subjected to the lysing step.

If the Applicants' steps are broken into an agglutination step and a lysis step and then applied to the teachings of Doshi and Zierdt, the result is different. The Applicants teach a first filter of about 2 – 20 μm. If a sample is taken and introduced to an agglutinating agent and then passed over the filter, the Applicants capture the white blood cells (which are on average 25 μm). The resulting fluid is a plasma that is substantially free of cellular blood components. At this point, applying Zierdt (lysis) does not make sense as the main point of Zierdt is that assay sensitivity can be increased by lysis of the white blood cells which contain phagocytized bacteria. The Applicants would have just removed all the white blood cells in the previous step. Thus, the combination would not be made by one skilled in the art.

The Applicants respectfully submit that those teachings lead those skilled in the art away from the Applicants' claimed teachings. For example, even if one skilled in the art were to hypothetically combine Zierdt with Doshi, importing the teachings of Zierdt into Doshi would result in lysing of the entire blood sample, as opposed to lysing residual cells which is what the Applicants claim in Claims 1 – 5, 8, 10, 14 – 17, 23 – 27 and 37 – 38.

That assumes that one skilled in the art would make the combination in the first place. One of the goals of Doshi is to remove blood cells from whole blood since it is difficult to conduct analysis of dissolved blood components without interference from the red blood cells. Doshi suggests applying a secondary filter with a very small particle size to rid the resulting blood cells of the first agglutination/filtration. There is no need for the lysis of red cells in Doshi since debris of red cells causes interference to the analysis of dissolved blood components such as is discussed in col. 2, line 12 of Doshi. Thus, the Applicants respectfully submit that hypothetically combining Zierdt with Doshi would lead one skilled in the art away from the Applicants' claimed selective lysing of residual cells of a filtrate.

The rejection also turns to Aunet for the proposition that it would be obvious to utilize an Aunet-type device which comprises an enclosed and sterile housing. As noted in the previous Response, there is no such disclosure of an enclosed and sterile housing given the components that are open to the surrounding environment. Thus, importing the teachings of Aunet into the teachings of Zierdt and Doshi would still not cure that deficiency with respect to the enclosed and sterile device.

Moreover, importing the teachings of Aunet into Zierdt and Doshi would not cure the deficiencies set forth above with respect to selectively lysing residual cells of a filtrate. Aunet suggests that "no surfactant should be present in such concentrations as to cause hemodialysis of the red blood cells" in col. 4, lines 26 – 28. Thus, Aunet discourages utilization of lysis to separate blood cells from whole blood.

The Applicants' process is remarkable in that it is performed directly on a sample stemming from a blood product collected from a subject without prior treatment or dilution, as discussed in the Applicants' specification. Indeed, in the test of the prior art for detecting pathogenic microbes in blood products, the treatments that are supposed to selectively extract the pathogenic microbes simultaneously cause an elimination of these microbes. This elimination leads to an underassessment of the presence of the microbes in the blood product. The Applicants' method, as defined in Claim 1, allows detecting contaminating microbes without underestimating their presence. None of Doshi, Aunet and Zierdt teaches or suggests such a method. For that reason also, the subject matter of Claim 1 involves an inventive step.

Aunet does not disclose, teach or suggest a device comprising an enclosed and sterile housing, entry and exit ports. Aunet discloses that "a sample of whole blood is applied to an inlet or first end of the matrix" (col. 5, lines 48 – 49). This inlet is not disclosed as being enclosed and sterile. Indeed, none of the terms "enclosed," "sterile," "safe," "pollution" or "contaminant" is

used in Aunet. In addition, each figure of Aunet shows an inlet of the entry port which is in contact with the external environment (col. 5, lines 65 to col. 7, line 63, and references 14, 34, 74 and 94 of Figs. 1 – 5). It can be seen on those figures that the inlet is not enclosed in the device. The device of Aunet is not enclosed and cannot be sterile. In fact, nothing in Aunet or Doshi or Zierdt suggests conducting the process in an enclosed and sterile device. Consequently, there is a risk in Aunet of extraneous microbe induction in the sample to analyze. Further, there is no indication of how to avoid external contamination disclosed in this document.

In the Applicants' method, there is no possibility of external contamination since the method is performed in an enclosed and sterile device. The rejection states that one skilled in the art performing analysis on blood or blood products would perform the assay within a sterile and enclosed hood. Such an art is typical of the prior art. The Applicants' method allows the user to be free of a hood. Thus, the Applicants' method can be used anywhere since the device in which it is performed is enclosed and sterile. For this reason also, the subject matter of Claim 1 involves an inventive step.

Thus, the notion in the rejection that the Applicants' method is performed in an enclosed and sterile device is equivalent of being performed under a hood is clearly in error. It is not necessary to perform the claimed method under a hood.

The Applicants therefore respectfully submit that one skilled in the art would not make the hypothetical combination of Zierdt with Aunet and Doshi and that, in any event, the combination would still fail to result in the subject matter of Claims 1 – 5, 8, 10, 14 – 17, 23 – 27 and 37 – 38.

Claims 6 and 7 stand rejected under 35 USC §103 over the further hypothetical combination of Cathey with Zierdt and Doshi. The Applicants respectfully submit that Cathey

fails to cure the deficiencies set forth above with respect to Zierdt and Doshi. Withdrawal of the rejection is respectfully requested.

Claims 9 and 13 stand rejected under 35 USC §103 over the further hypothetical combination of Besson-Faure with Zierdt, Aunet and Doshi. The Applicants respectfully submit that Besson-Faure fails to cure the deficiencies set forth above with respect to Zierdt, Aunet and Doshi. Withdrawal of that rejection is also respectfully requested.

In light of the foregoing, the Applicants respectfully submit that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,

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